UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/529,053	04/06/2000	James W. Williams	29666/35415	1413

7590 12/15/2005

Marshall O'Toole Gerstein
Murray & Borun
6300 Sears Tower
233 South Wacker Drive
Chicago, IL 60606-6402

EXAMINER	
WANG, SHENGJUN	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 12/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/529,053	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted August 24, 2005 is acknowledged. In view of the decision by Board of patent appeals and interferences mailed June 22, prosecution in hereby reopened.

Claims Objections

1. Claims 28 and 29 are objected to because of the following informalities:

claim 28 recite "hydroxycrotonamde" which appears to be a typographic error of "hydroxycrotonamide."

Claim 29 recited "claim 25". It is noted that claim 25 has been cancelled. It appears to be a typographic error for "claim 26" For expedient prosecution, the claims has been examined as it depends on claim 26.

Appropriate correction is required.

Claim Rejections 35 U.S.C. 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 26, 27, 29-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Weithmann et al.

3. Reading the claims in light of the specification, the claims are construed as require administration of leflunomide, its active metabolite, related derivatives, or anti-viral active metabolites thereof, to a human in an amount effective to inhibit viral virion assembly, such amounts can very from 0.1 mg/day to 80 mg/day. (see pages 13-19). Note the human herein may be either infected, or not infected with the viruses. The claims read on both treatment of prophylactic treatment of viral infection (see the discussion in Board's decision, pages 4-5 in particular).

1. Weithmann et al. teach a method of treating disorder in which interleukin 1 beta is involved. The disorders include viral infections, such as HIV or hepatitis, comprising administering leflunomide to the patient. See, particularly, the abstract and the claim. The dosage may range from 3-50 mg daily, but may be higher if required. See, particularly, column 3, lines 7-16. Note, treating HIV patient would have inherently provided a prophylactic treatment against herpes viral infection, other any other viral infection. As to the limitation "to inhibit viral virion assembly," The instant claims are directed to effecting a biochemical pathway with an old and well known compounds. The argument that such claims are not directed to the old and well known ultimate utility (treating viral infection) for the compounds, e.g., leflunomide, are not probative. It is well settled patent law that mode of action elucidation does not impart patentable moment to otherwise old and obvious subject matter. Applicant's attention is directed to In re Swinehart, (169 USPQ 226 at 229) where the Court of Customs and Patent Appeals stated "is elementary that the mere recitation of a newly discovered function or property, inherently possessed by thing in the prior art, does not cause a claim drawn to those things to distinguish

over the prior art." In the instant invention, the claims are directed to the ultimate utility set forth in the prior art, albeit distanced by various biochemical intermediates.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 26, 27, 29, 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weithmann et al. (US Patent 5,556,870).

3. Weithmann et al. teach a method of treating disorder in which interleukin 1 beta is involved. The disorders include viral infections, such as HIV or hepatitis, comprising administering leflunomide to the patient. See, particularly, the abstract and the claim. The dosage may range from 3-50 mg daily, but may be higher if required. See, particularly, column 3, lines 7-16.

2. Weithmann et al. does not teach expressly the amount effective to inhibit viral virion assembly. However, the optimization of a result effective parameter, e.g., effective amount for a therapeutical dosage of a known therapeutical agent, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215. Further, treating a disease with an agent in a host would lead the agent contacting the pathogenic cell. A method known to be useful for treating viral infection would have been reasonably expected to be useful for prophylactic purpose. Finally, since leflunomide is effective against virus through different mechanism, it

would have been reasonably expected to effective against those virus with resistance to antiviral agent that inhibit viral DNA replication. As to the limitation "for inhibiting viral replication in cells," note the functional limitation of the method is not seen to make the otherwise obvious method patentable distinct. The instant claims are directed to effecting a biochemical pathway with an old and well known compounds. The argument that such claims are not directed to the old and well known ultimate utility (treating viral infection) for the compounds, e.g., leflunomide, are not probative. It is well settled patent law that mode of action elucidation does not impart patentable moment to otherwise old and obvious subject matter. Applicant's attention is directed to In re Swine hart, (169 USPQ 226 at 229) where the Court of Customs and Patent Appeals stated "is elementary that the mere recitation of a newly discovered function or property, inherently possessed by thing in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." In the instant invention, the claims are directed to the ultimate utility set forth in the prior art, albeit distanced by various biochemical intermediates. The ultimate utility for the claimed compounds is old and well known rendering the claimed subject matter obvious to the skilled artisan. It would follow therefore that the instant claims are properly rejected under 35 USC 103.

Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weithmann et al. (US Patent 5,556,870) in view of Flamand et al.

Claim 30 is obvious for reasons discussed above and in further view of Flamand et al. Weithmann et al. do not teach expressly the method for treating herpes.

4. However, Flamand et al. teaches that herpes infection is involved with interleukin 1 beta. See, particularly, the abstract.

5. Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ the method of Weithmann for treating herpes infections.

6. A person of ordinary skill in the art would have been motivated to employ the method of Weithmann for treating herpes infections, because herpes infection is known to be involved interleukin 1 beta.

7. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weithmann et al. (US Patent 5,556,870) in view of Hammer (AIDS 1996, vol. 10, suppl 3, s1-s11).

8. Claim 34 is obvious over Weithmann et al. as discussed above, and further in view of Hammer (AIDS 1996, vol. 10, suppl 3, s1-s11).

Weithmann et al. do not teach expressly the employment of addition antiviral agent in the method.

9. However, Hammer teaches that several pyrimidin compounds are known antiviral agents. See, particularly, page s3.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a combination of leflunomide compounds with other antiviral agents such as those known pyrimidin compounds Also, it is prima facie obvious to combine two compositions each of which is taught in the prior art to be useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in

prior art; thus , the claimed invention which employ a combination of two known anti-viral agents sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. Further, combination therapies for viral infection are known to be better than single agent therapy. See, Hammer, page s2, the paragraph of combination therapy.

Claims 26-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coghlan et al. (WO 94/24095) in view of McChesney et al. (Transplantation, Vol. 57, no. 12, page 1717-1722).

10. Coghlan et al. teaches compounds with general structures that encompass leflunomide or its active metabolite, the compounds have similar biological activity of leflunomide or its metabolite. See, particularly, the abstract, page 2, the examples and the claims. The expressly taught compounds includes those meet the leflunomide products (page 18-19 in the specification). Homologue of leflunomide (e.g., 5-methyl-isoxazole-4-carboxylic acid 2,2,2,trifloroethylamide) have been expressly disclosed (page 10, line 35). These compounds are known to be useful for treating or preventing viral infection such as hepatitis and cytomegalovirus infection, particularly, HCMV. See, page 4, lines 23-32.

11. Coghlan et al. does not teach expressly the employment leflunomide or its metabolite, or the particular amount herein for treating viral infections.

12. However, McChesney et al. teaches that both leflunomide and A771726 are known to be effective in preventing viral infection. See, particularly, the abstract at page 1717, and the materials and method at page 1717-1718.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ the compounds taught by Coghlan et al., including both leflunomide and A771726, for treating or prevention viral infections such as hepatitis and CMV.

3. A person of ordinary skill in the art would have been motivated to employ the compounds taught by Coghlan et al., including both leflunomide and A771726, for treating or prevention viral infections such as hepatitis and CMV because these compounds are known to be useful for treating or preventing viral infection, and both leflunomide and A771726 are known to be similarly useful as the other compounds. Further the reference teaches certain compounds that are structural homologs of the instantly claimed leflunomide, i.e., they differ only by a CH_2 group. The instant compounds are structural homologs of the reference compounds when they differ only by a CH_2 group. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compound because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. In re Hass, 60 USPQ 544 (CCPA 1944); In re Henze, 85 USPQ 261 (CCPA 1950). Finally, since leflunomide is effective against virus through different mechanism, it would have been reasonably expected to effective against those virus with resistance to antiviral agent that inhibit viral DNA replication. As to the limitation "for inhibiting viral replication in cells," note the functional limitation of the method is not seen to make the otherwise obvious method patentable distinct. The instant claims are directed to effecting a biochemical pathway with an old and well known compounds. The argument that such claims are not directed to the old and

well known ultimate utility (treating viral infection) for the compounds, e.g., leflunomide, are not probative. It is well settled patent law that mode of action elucidation does not impart patentable moment to otherwise old and obvious subject matter. Applicant's attention is directed to In re Swinehart, (169 USPQ 226 at 229) where the Court of Customs and Patent Appeals stated "is elementary that the mere recitation of a newly discovered function or property, inherently possessed by thing in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." In the instant invention, the claims are directed to the ultimate utility set forth in the prior art, albeit distanced by various biochemical intermediates. The ultimate utility for the claimed compounds is old and well known rendering the claimed subject matter obvious to the skilled artisan. It would follow therefore that the instant claims are properly rejected under 35 USC 103.

Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Coghlan et al. (WO 94/24095) in view of McChesney et al. (Transplantation, Vol. 57, no. 12, page 1717-1722), and further in view of Hammer (AIDS 1996, vol. 10, suppl 3, s1-s11).

Coghlan et al. (WO 94/24095), and McChesney et al. do not teach expressly the employment of addition antiviral agent in the method.

13. However, Hammer teaches that several pyrimidin compounds are known antiviral agents. See, particularly, page s3.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to employ a combination of leflunomide compounds with other antiviral agents such as those known pyrimidin compounds Also, it is prima facie obvious to combine two compositions each of which is taught in the prior art to be

useful for same purpose in order to form third composition that is to be used for very the same purpose; idea of combining them flows logically from their having been individually taught in prior art; thus , the claimed invention which employ a combination of two known anti-viral agents sets forth prima facie obvious subject matter. See In re Kerkhoven, 205 USPQ 1069. Further, combination therapies for viral infection are known to be better than single agent therapy. See, Hammer, page s2, the paragraph of combination therapy.

Response to the Arguments

Applicants' amendments and remarks submitted August 24, 2005 have been fully considered, but are unpersuasive.

14. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

15. Applicants arguments that Weithmann et al. do teach any anti-viral effect is untenable. Weithmann et al. particularly claim the method of using leflunomide for treating HIV, hepatitis. As discussed above, a particular new mechanism of an otherwise old and well-known method does not render the old method patentable distinct.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

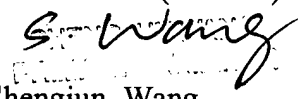
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Shengjun Wang
Primary Examiner
Art Unit 1617